ISOTOPES FOR CONTROL OF HUMAN COMMUNICABLE DISEASES (RAF/6/017) E1

New

MODEL PROJECT

CORE FINANCING

YEAR	Experts		Group Activity	Equipment	Fellowships		Scientific Visits		Group Training	Sub-Contracts	Misc. Comp.	TOTAL
	m/d	US $	US $	US $	m/d	US $	m/d	US $	US $	US $	US $	US $
1997	2/0	26,400	0	215,000	0/0	0	0/0	0	46,200	60,000	0	347,600
1998	2/0	27,900	0	60,000	0/0	0	0/0	0	32,550	60,000	0	180,450
1999	3,0	44,100	0	80,000	0/0	0	0/0	0	0	60,000	0	184,100

First Year Approved 1997

OBJECTIVES: This project addresses the regional development objective of more effectively managing two widespread communicable diseases, malaria and tuberculosis. The specific project objectives are to enhance the capabilities of health centres to diagnose and control malaria and tuberculosis through the use of radionuclide-based molecular techniques.

BACKGROUND: The rising incidence of communicable diseases has become a major problem in sub-Saharan Africa, exacerbated by the advent of HIV. It is not only a major cause of death but also leads to increased incidence of tuberculosis (TB). The TB infection rate now exceeds 100 per 100,000 inhabitants in most countries. Annually 1,500,000 new cases and 600,000 TB deaths occur. Furthermore, malaria is still the largest cause of mortality in Africa, particularly in children. Each year about 1.8 million people die of malaria on the continent, of whom 30% are children. The health and economic consequences of malaria are considerable. According to WHO, the combined direct and indirect cost of the disease was US $1.8 billion in 1995. The prevailing situation has prompted the United Nations to include basic health care as one of the 14 components for action under the newly launched ten-year systemwide Special Initiative on Africa. The initiative aims at strengthening national health systems and promoting country ownership of health programmes with a view to improving diagnostics and treatment of communicable diseases. Escalation of disease prevalence is making increasing demands on resources available to the health sector. Even so, most countries continue to operate control programmes for many diseases, based on the provision of relatively low-cost therapeutic drugs. Strains of tuberculosis and malaria pathogens have emerged which are resistant to many drugs. The AIDS-related pathogenicity of common mycobacteria makes further demands on available resources. Both are major obstacles to effective national control programmes. More efficient use of scarce resources is possible through early specific identification of the pathogen, and rapid assessment of its susceptibility to drugs. The past decade has seen the development of molecular techniques using radionuclide tracers that provide sensitive and rapid methods of infection diagnosis and detection of drug-resistant pathogens. Many of the methods rely on DNA methodology, which is making an impact on diagnostic procedures similar to that of radioimmunoassay in the 1960s. Methods such as Southern blot, restriction fragment length polymorphism (RFLP) and single-strand confrontation polymorphism (SSCP) all use the radionuclide phosphorus-32 to greatly enhance sensitivity. Use of the isotope facilitates detection of the minor differences in DNA sequences that distinguish drug-resistant from drug-susceptible pathogens. Their species, strain, and even clone are identifiable. The methods are not only valuable in clinical diagnosis and epidemiology. They are also amenable to the rapid batch analysis needed with large numbers of samples in national surveillance programmes. They clearly have the potential for making a major contribution to the control of communicable diseases.

PROJECT PLAN: Following extensive consultations with Member States and important technical preparatory work, a regional meeting took place on 1–4 April 1996 in Nairobi, Kenya, to formulate a regional project for consideration in the 1997-98 regular TC programme. The meeting was hosted by the Kenya Medical Research Institute (KEMRI) and attended by participants from Kenya, Sudan, Tanzania, Zambia and Zimbabwe, representing medical institutions and ministerial primary health care services. The participants reviewed national diagnosis and control programmes on malaria and tuberculosis under implementation in target countries. Discussion focused on the applicability of isotope-based techniques under current control strategies, and on their advantages over other available methodologies. Drug resistance emerged as the major obstacle to national control programmes. Regular surveillance of resistance to the routinely used drugs is essential for the success of national control programmes. The conventional methods are slow, labour intensive and often unreliable. In contrast, radionuclide-based techniques are rapid, sensitive and reliable. This project will put them into use by reference laboratories for clinical detection of drug-resistant forms of the two diseases and in epidemiological surveillance. Principal diagnostic institutes in Kenya, Mali, Sudan, Tanzania, Zambia and Zimbabwe will participate in the project. These institutes are well equipped; the project will provide only the limited amount of equipment and reagents necessary to upgrade the facilities for radionuclide-based methods. One or two centres in South Africa will also participate in the project to provide technical support. Two regional training courses are scheduled. The first (two-week) course will train two junior staff members from each institute in radionuclide-based methods for drug resistance surveillance. The second (one-week) course will train the principal counterpart from each of the six countries. An expert will make short (one to two weeks) visits to those institutes having difficulties in using the techniques. Pilot studies to validate the techniques will take place in the first year. Pilot studies will also take place at KEMRI, Nairobi, and the School of Medicine, Bamako, on the use of tritiated chloroquine and the calcium blocker Verapamil in the rapid test to determine resistance of malaria parasite strains to chloroquine. During the second year, if the mutation for chloroquine resistance is still unknown, the use of the rapid test for chloroquine may be extended to all six institutes. Extensive field validation of the other techniques will continue, including a comparison of the cost effectiveness of these methods vis-à-vis conventional and non-isotopic procedures. A regional training course for junior staff will take place in the second year, including participants from institutes not participating in the project. During the third year, the techniques established during the first two years will come into routine use for clinical detection of drug-resistant forms of the two diseases and in epidemiological surveillance. In each country, the participating institute will collaborate with the Ministry of Health and national health-care centres to utilize the results obtained. There will also be regional co-ordination and co-operation through annual meetings, external quality assurance, sharing of information and exchange of expertise. The development of one of the six institutes as a regional centre able to synthesize primers and probes for all is under consideration. Incorporating this regional reagent production facility into the project will reduce costs of reagents and lead to sustainability of national control programmes.

NATIONAL COMMITMENT: The six participating countries will provide appropriate infrastructure, qualified personnel and sufficient financial resources to achieve the establishment of radionuclide-based methodologies for detecting drug resistance.

AGENCY INPUT: The participating institutes have most of the necessary basic laboratory equipment, including in some cases equipment needed for molecular biology. A questionnaire will ascertain what essential equipment is needed at each laboratory, and funds of up to US $30,000 per laboratory will be earmarked for its purchase in the first year. In addition, each institute will receive reagents and consumable supplies to the total cost of US $10,000 per year. The two centres evaluating the rapid test for chloroquine resistance are fully equipped for the test, except that a liquid scintillation counter is required at KEMRI. Three regional training courses will take place during the first two years of the project, and co-ordination meetings will convene during the second and third years. Expert missions will assist any institutes initially unable to use the techniques envisaged.

PROJECT IMPACT: Improved methods for monitoring drug resistance in malaria and tuberculosis will lead to better case management and to lower morbidity and mortality. This should not only lower the cost of managing such diseases, but also improve productivity and the quality of life for the communities the project benefits. The reliability and speed associated with these techniques will enable health care centres to make more effective and efficient use of the financial resources available for disease treatment and control.